Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A composition comprising ~~at least one human papillomavirus (HPV) peptide;~~ an oligopeptide 13 residues or less in length, which ~~the peptide comprising an isolated, prepared epitope consisting of a sequence selected from the group consisting of the sequences set out in Tables VII-XVIII that show a relative binding ratio of 0.01 or higher for at least one allele-specific HLA molecule~~comprises the sequence ATLERTEVY (SEQ ID NO:31040).

2. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is joined to an amino acid linker.

3. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is admixed or joined to a CTL epitope.

4. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is admixed or joined to an HTL epitope.

5. (Original) A composition of claim 4, wherein the HTL epitope is a pan-DR binding molecule.

6. (Currently amended) A composition of claim 1, further comprising a liposome, wherein the oligopeptide ~~epitope~~ is on or within the liposome.

7. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is joined to a lipid.

8. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is a heteropolymer.

9. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is a homopolymer~~homoplymer~~.

10. (Currently amended) A composition of claim 1, wherein the oligopeptide ~~epitope~~ is bound to an HLA heavy chain, β2-microglobulin, and strepavidin complex, whereby a tetramer is formed.

11. (Withdrawn) A composition of claim 1, further comprising an antigen presenting cell, wherein the epitope is on or within the antigen presenting cell.

12. (Withdrawn) A composition of claim 11, wherein the epitope is bound to an HLA molecule on the antigen presenting cell, whereby when a cytotoxic T lymphocyte (CTL) that is restricted to the HLA molecule is present, a receptor of the CTL binds to a complex of the HLA molecule and the epitope.

13. (Withdrawn) A composition of claim 11, wherein the antigen presenting cell is a dendritic cell.

14. (Currently amended) A composition comprising one or more peptides, and further comprising at least two oligopeptides 13 residues or less in length, ~~epitopes, wherein one of the~~ wherein the first oligopeptide comprises ~~epitopes is selected from the group consisting of sequences set out in Tables VII-XVIII that show a relative binding ratio of 0.01 or higher for at least one allele-specific HLA molecule~~ the sequence ATLERTEVY (SEQ ID NO:31040); and

wherein each of said one or more peptides comprise less than 50 contiguous amino acids ~~that have 100% identity with~~ of a native peptide sequence of human papilloma virus (HPV) strains 16, 18, 31, 45, 33, and 56.

15. (Currently amended) A composition of claim 14, wherein one peptide comprises the at least two oligopeptides ~~epitopes~~.

16. (Original) A composition of claim 14, wherein at least one of the one or more peptides is a heteropolymer.

17. (Original) A composition of claim 14, wherein at least one of the one or more peptides is a homopolymer.

18. (Currently amended) A composition of claim 14, further comprising an additional oligopeptide ~~epitope~~.

19. (Currently amended) A composition of claim 18, wherein the additional oligopeptide ~~epitope~~ is derived from a tumor associated antigen.

20. (Currently amended) A composition of claim 18, wherein the first oligopeptide ~~epitope~~ is joined to a cytotoxic T lymphocyte (CTL) epitope.

21. (Currently amended) A composition of claim 18, wherein the first oligopeptide~~epitope~~ is joined to a helper T lymphocyte (HTL) epitope.

22. (Original) A composition of claim 21, wherein the HTL epitope is a pan-DR binding molecule.

23. (Currently amended) A composition of claim 14, further comprising a liposome, wherein the first oligopeptide ~~epitope~~ is on or within the liposome.

24. (Currently amended) A composition of claim 14, wherein the first oligopeptide~~epitope~~ is joined to a lipid.

25. (Withdrawn) A composition of claim 14, further comprising an antigen presenting cell, wherein the epitope is on or within the antigen presenting cell.

26. (Withdrawn) A composition of claim 25, wherein the epitope is bound to an HLA molecule on the antigen presenting cell, whereby when a cytotoxic lymphocyte (CTL) that is restricted to the HLA molecule is present, a receptor of the CTL binds to a complex of the HLA molecule and the epitope.

27. (Withdrawn) A composition of claim 25, wherein the antigen presenting cell is a dendritic cell.

28. (Original) A composition of claim 14, further comprising an additional peptide admixed with the one or more peptides.

29. (Original) The composition of claim 28, wherein the additional peptide comprises a CTL or HTL epitope.

30. (Currently amended) A ~~vaccine~~ composition comprising:

a unit dose of a peptide that comprises less than 50 contiguous amino acids ~~that have 100% identity with~~ of a native peptide sequence of human papilloma virus (HPV) strain 45 ~~(HPV) strains 16, 18, 31, 45, 33, and 56~~, the peptide comprising the sequence ATLERTEVY (SEQ ID NO:31040) ~~an epitope selected from the group consisting of sequences set out in Tables VII-XVIII that show a relative binding ratio of 0.01 or higher for at least one allele-specific HLA molecule~~; and;

a pharmaceutical excipient.

31. (Currently amended) A ~~vaccine~~ composition in accordance with claim 30, further comprising an additional epitope.

32. (Currently amended) A ~~vaccine~~ composition of claim 31, wherein the additional epitope is a PanDR binding molecule.

33. (Currently amended) A ~~vaccine~~ composition of claim 30, wherein the pharmaceutical excipient comprises an adjuvant.

34. (Withdrawn) A vaccine composition of claim 30, further comprising an antigen presenting cell.

35. (Withdrawn) A vaccine composition of claim 34, wherein the epitope is bound to an HLA molecule on the antigen presenting cell, whereby when a cytotoxic T lymphocyte (CTL) that is restricted to the HLA molecule is present, a receptor of the CTL binds to a complex of the HLA molecule and the epitope.

36. (Withdrawn) A vaccine composition of claim 35, wherein the antigen presenting cell is a dendritic cell.

37. (Currently amended) A ~~vaccine~~ composition of claim 30, further comprising a liposome, wherein the at least one epitope is on or within the liposome.

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-10, 14-24, 28-33, and 37 are pending in the application, with 1, 14, and 30 being the independent claims. Claims 11-13, 25-27, and 34-36 have been withdrawn by the Examiner.[1]

Support for the amendment of claims 1-4, 6-10, 14-15, 18-21, and 23-24 can be found in the specification, for example, at page 13, lines 1-9.

Applicants have amended the specification to direct the entry of a Substitute Sequence Listing at the end of the application. The Substitute Sequence Listing contains a sequence from page 52 of the specification as SEQ ID NO: 51505. The Substitute Sequence Listing is submitted herewith on compact disc in accordance with 37 C.F.R. § 1.821(c) and (e). The required duplicate copies of the written form on compact disc are labeled "Copy 1 Replacement 07/14/2003" and "Copy 2 Replacement 07/14/2003". The computer readable form of the Substitute Sequence Listing is also submitted on compact disc, labeled "Computer Readable Format".

Each compact disc containing the Substitute Sequence Listing is formatted for IBM-PC, ASCII DOS text. The three discs each contains one file: Substitute Sequence Listing 2060_0100001, 11,283,155 bytes, created on October 17, 2003.

In compliance with 37 C.F.R. § 1.52(e)(4) the duplicate copies of the written form on compact disc and the computer readable form of the Substitute Sequence Listing on

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[1]The Office Action did not indicate the status of claim 37. Applicants note that claim 37 is part of Group I, the elected invention, and is therefore pending.

compact disc are identical, *i.e.*, "Copy 1 Replacement 10/17/2003" and "Copy 2 Replacement 10/17/2003" are identical, and the sequence information recorded in computer readable form on compact disc, *i.e.*, "Computer Readable Format" is identical to the written (on compact disc) Substitute Sequence Listing. In compliance with 37 C.F.R. § 1.52(e)(4) the replacement compact disc contains no new matter.

The specification has been amended, in accordance with 37 C.F.R. § 1.52(e)(5) to incorporate by reference the Substitute Sequence Listing submitted herewith on Compact Disc.

The specification has also been amended to add a sequence identifier on page 52.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1-10, 14-24, and 29-30 under 35 U.S.C. § 112, second paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Paper No. 18, page 3. Applicants respectfully traverse the rejection.

The Examiner states that "[i]t is not clear in claim 1 what the metes and bounds of the size of 'epitope' is." Paper No. 18, page 3. Applicants have amended independent claim 1 to clarify that the composition comprises an "oligopeptide 13 residues or less in

length."[2] Claims 2-10 depend from claim 1, and therefore include the same length limitation. Likewise, Applicants have amended independent claim 14 to clarify that the composition comprises an "oligopeptide 13 residues or less in length." Claims 15-24 and 28-29, depend from claim 14, and therefore include the same length limitation. The amendment renders this portion of the rejection moot.

With respect to claim 30, Applicants point out that the claim includes a length limitation.

The Office Action also states that, in claims 8 and 9, the terms "heteropolymer" and "homopolymer" are not defined in the specification and it is not clear what the metes and bounds of the terms are. Paper No. 18, page 3. Applicants note that "heteropolymer" and "homopolymer" are disclosed in the specification on page 46, at lines 3-12, which states:

> Alternatively, the peptide can exist as a homopolymer comprising multiple copies of the same peptide, or as a heteropolymer of various peptides. Polymers have the advantage of increased immunological reaction and, where different peptide epitopes are used to make up the polymer, the additional ability to induce antibodies and/or CTLs that react with different antigenic determinants of the pathogenic organism or tumor-related peptide targeted for an immune response.

Even in the absence of this disclosure at page 46, Applicants respectfully assert that one of ordinary skill in the art, based on the specification as a whole, would understand that a homopolymer is a protein or peptide comprising multiple copies of the same epitope, and a heteropolymer is a protein or peptide comprising various different epitopes. Therefore, the

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[2]Applicants have amended the claims to refer to an "oligopeptide" rather than an "epitope."

metes and bounds of the terms "homopolymer" and "heteropolymer" would be understood by the artisan of ordinary skill.

The Office Action further states that in claim 30 it is not clear what the unit dose is. Paper No. 18, page 3. Applicants assert that the term "unit dose" is well-known to those of ordinary skill in the art, and thus is clear on its face. In fact, according to a publication of an agency of the U.S. Department of Health and Human Services, "unit-dose dispensing of medication was developed in the 1960's" and is now "a standard practice at hospitals in the United States." Making Health Care Safer: A Critical Analysis of Patient Safety Practices, AHRQ Publication No. 01-E058 available at http://ahcpr.gov/clinic/ptsafety/. Unit dose is defined as "occurring in or using a single dose, seen as a standard of measurement" (*See* http://www.medical-dictionary.com and http://cancerweb.ncl.ac.uk/omd/).

Furthermore, the specification defines what a unit dose is for therapeutic immunization purposes, for example, on page 58, lines 16-19. Applicants respectfully assert that one of ordinary skill in the art would understand the term "unit dose." Therefore, claim 30 is clear and definite.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 30-33 under 35 U.S.C. § 112, first paragraph, allegedly "because the specification, while being enabling for stimulating CTL response in vitro, does not reasonably provide enablement for vaccines." Paper No. 18, page 4. Applicants have amended claims 30-33 to claim a "composition" rather than a "vaccine

composition." Thus, the rejection has been rendered moot. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1-10, 14-24, and 28-33 under 35 U.S.C. § 103(a) as allegedly being obvious over Kubo, *et al.* (U.S. Patent No. 6,037,135) and an NCBI Sequence listing. Applicants respectfully traverse this rejection.

The subject matter of Kubo, *et al.* and the subject matter of the pending claims were commonly owned or under an obligation of assignment to the same entity at the time the subject matter of the pending claims was invented.[3] The present application was filed after November 29, 1999. Therefore, Kubo *et al.* is not available as prior art under 35 U.S.C. § 102(e), (f), or (g) to establish obviousness of the present claims. *See* 35 U.S.C. § 103(c) and MPEP 706.02(l)(1) and (2).

Applicants reserve the right to disqualify as prior art the subject matter of the NCBI Sequence listing reference under 35 U.S.C. § 103(c). However, even assuming, arguendo, that this cited reference is available as prior art, Applicants submit that the claimed invention is nonobvious over it.

Applicants also assert that even if Kubo *et al.* is available as art under 35 U.S.C. § 102(e), the pending claims are not obvious over Kubo *et al.* in view of the NCBI

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[3] The assignment for the Kubo *et al.* patent (U.S. Appl. No. 08/159,339) is recorded at Reel 6850, Frame 0221 to Cytel Corporation. A transfer of ownership from Cytel Corporation to Epimmune Inc. for the 08/159,339 application is recorded at Reel 9167, Frame 0827. The assignment to Epimmune Inc. for the current Application No. 09/641,528 is recorded at Reel 011705, Frame 0182.

Sequence listing . To establish a *prima facie* case of obviousness, a prior art reference must teach and suggest each and every claim limitation. M.P.E.P. 2143. Furthermore, for chemical entities claimed in structural terms, "a *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art." *In re Deuel*, 34 U.S.P.Q.2d 1210, 1214 (Fed. Cir. 1995). The instant claims recite a specific HPV 45 E6 peptide. Therefore, the patent relied on by the Examiner must teach or suggest each amino acid of this peptide.

In *In re Deuel*, the court held that generic DNA sequences encoding a particular protein were patentable over the prior art disclosure of a partial amino acid sequence and a general method of isolating DNA. *Deuel*, 34 U.S.P.Q.2d 1210. The court reasoned, "[t]he fact that one can conceive a general process in advance for preparing an *undefined* compound does not mean that a claimed *specific* compound was precisely envisioned and therefore [unpatentable]." *Id.* at 1216.

Here, the Examiner relies upon the Kubo *et al.* patent and the NCBI Sequence Listing. Kubo *et al.* discloses a general method of selecting peptides of having particular HLA motifs. Kubo *et al.* does not disclose the particular structural information for the specific peptide recited in the claims. The NCBI Sequence Accession No. X74479 discloses a 7858 bp linear HPV45 genomic DNA sequence. This reference does not disclose the specific claimed peptide. Additionally, assuming that Kubo *et al.* teaches or suggests a genus of peptides, it is well-established that a genus does not render obvious one particular species, absent some teaching or suggestion to arrive at the claimed structure. *In re Lalu*, 747 F.2d 703, 705 (Fed. Cir. 1984); M.P.E.P 2144.08 II.A.4, at 2100-143. Therefore, the

claimed peptide cannot be rendered obvious over Kubo *et al.* and the NCBI Sequence Listing.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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